Early industry/HTA Collaboration: Can we afford not to do it?

Dr Bernard Prigent
Vice President & Medical Director
Pfizer Canada
April 17, 2012
Current R&D Productivity is Alarming

Figure 2.6  Innovation Gap: R&D Investments Versus New Drug Approvals

Source: Burrill & Company
Scientific Advances: Can Innovation Master Master Complexity?

5-Yr Survival Blood Cancers ~0% Today 70%

100 years ago | Disease of the blood

80 years ago | Understanding of leukemia and lymphoma as cancers

60 years ago | Chronic leukemia
Acute leukemia
Preleukemia
Indolent lymphoma
Aggressive lymphoma

Today | ~38 leukemia types identified:
• Acute myeloid leukemia (~12 types)
• Acute lymphoblastic leukemia (2 types)
• Acute promyelocytic leukemia (2 types)
• Acute monocytic leukemia (2 types)
• Acute erythroid leukemia (2 types)
• Acute megakaryoblastic leukemia
• Acute myelomonocytic leukemia (2 types)
• Chronic myeloid leukemia
• Chronic myeloproliferative disorders (5 types)
• Myelodysplastic syndromes (6 types)
• Mixed myeloproliferative/myelodysplastic syndromes (3 types)

51 lymphomas identified:
• Mature b-cell lymphomas (~14 types)
• Mature T-cell lymphomas (15 types)
• Plasma cell neoplasm (3 types)
• Immature (precursor) lymphomas (2 types)
• Hodgkin’s lymphoma (5 types)
• Immunodeficiency-associated lymphomas ~ 5 types)
• Other hematolymphoid neoplasm’s (~7 types)


Pfizer
Oncology: Pfizer Programs
(last 5 years)

INNOVATION: Can we have more shots on goals?

SUCCESSFUL

FAILED

Sunitinib MRCC

Sunitinib PNeT

Crizotinib NSCLC ALK+

Axitinib MRCC

A4021016 Figitumumab Metastatic lung cancer 1st line

A6181122: Colorectal Cancer

CAM Refractory Gastric cancer

A6181087 SUT Metastatic Lung cancer 2nd line

A6181077: phase 2 head to head in triple negative breast cancer

A3671009 TRE Metastatic Melanoma 1st line

CAM -Small Cell Lung cancer

A6181084 SUT Metastatic Lung cancer 1st line

CAM Adjuvant treatment of colorectal cancer

A618120: Prostate Cancer

A6181170: Hepato-cellular Carcinoma

A4061028: Adeno-carcinoma of the pancreas

A4021018 Figitumumab Metastatic lung cancer 2nd line

A6181064: 1st line MBC

A6181099: 2nd line MBC

TLR-9 antagonist in Metastatic Lung cancer

A4021016 Figitumumab Metastatic lung cancer 1st line

TRE Metastatic Melanoma 1st line

TRE Metastatic Lung cancer 2nd line

TRE Met Colorectal

TRE Pancreatic cancer

CI-1033 Met Breast

CI-1033 Met Lung

Figitumumab MBC

CI-1033 Met Breast

Figitumumab Colorectal

INNOVATION: Can we have more shots on goals?
Patients and Physicians Waiting for Treatments

- 8% of compounds entering Phase 1 will make it to market, down from 14% fifteen years ago

- Cost of development are escalating

- Failures due to lack of safety and/or efficacy

- Inability to predict failures

- Major barriers to address uncommon diseases and explore unproven technologies
# Alzheimer: Unchartered Pathways and Failures

<table>
<thead>
<tr>
<th>MOA</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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<tbody>
<tr>
<td><strong>Passive immunotherapy</strong></td>
<td>MABT5102A (mAb; Genentech)</td>
<td>Ponezumab (PF-04360365) (mAb; Pfizer)</td>
<td>Bapineuzumab (AAB-001; JAI/Pfizer)</td>
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<td></td>
<td>GSK933776A (mAb; GSK)</td>
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<td>IVlg 10% (IV human Immune Globulin; Baxter)</td>
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<td>AAB-003 (Pfizer)</td>
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<td>Solanezumab (mAb; Eli Lilly)</td>
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<td><strong>Vaccines</strong></td>
<td>V950 (vaccine; United Therapeutics)</td>
<td>ACC-001 (Conj.vaccine; JAI/Pfizer)</td>
<td>AN-1792 (Elan/Wyeth/Pfizer)</td>
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<td>UB311 (vaccine; United Merck)</td>
<td>CAD 106 (vaccine; Cytos/Novartis)</td>
<td>semagacestat (γ-secretase inhibitor; Eli Lilly)</td>
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<td>AFFITOPE AD03 (vaccine; Affiris)</td>
<td>AFFITOPE AD02 (vaccine; Affiris)</td>
<td>Flurizan (6HT1a Agonist; Myriad)</td>
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<td><strong>Aβ Production Inhibition</strong></td>
<td>GSI-953 (γ-secretase inhibitor; Pfizer)</td>
<td>CHF-5074 (γ-secretase inhibitor; Chieis Pharma)</td>
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<td>CTS21166 (β-secretase inhibitor CoMentis)</td>
<td>PF-0494700 (RAGE; Pfizer)</td>
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<td><strong>RAGE Inhibition</strong></td>
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<td><strong>Aβ Aggregation Inhibitor</strong></td>
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<td><strong>Other MOAs</strong></td>
<td>AZD3480 (NNR ag; AstraZeneca)</td>
<td>CERE-110: (NGF/adeboavirus; Ceregene)</td>
<td>Alzhemed (tramiprosate - Neurochem)</td>
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<td>SAM-760 (5HT6 anatag; Pfizer)</td>
<td>GSK-239512 (H3 anat; GSK)</td>
<td>Dimebon (Hist. antag++; Pfizer/Medivation)</td>
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<td>PF-04995274 (5HT4 anatag; Pfizer)</td>
<td>ST101 (unk; Sonexa)</td>
<td>Lecozotan (5HT1a Agonist; Wyeth/Pfizer)</td>
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<td>LNK 754 (Farnesyl trans inhibitor; Link Medicine Corp)</td>
<td>T-817MA (neurotrophic; Toyama)</td>
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<td>NRM8499 (tramiprosate prodrug Bellus)</td>
<td>PF-04447943 (PDE inhibitor; Pfizer)</td>
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<td>LuAE58054 (5HT6 anatag; Lundbeck)</td>
<td>TRx0014 (Tau; TauRx Therapeutics)</td>
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<td>ABT-384 (unk; Abbott)</td>
<td>HF0220 (steroid; Hunter-Fleming LTD)</td>
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What is the Real Value of Innovation?

Average % in a two-year period* of products with Full Listing Status
(for two-year periods ending Aug. 2008 to Aug. 2011)

Each data point represents a two-year average
Impact on Clinical Development

2 Examples of Pfizer Developmental Programs

- **Sulopenem**: pneumonia
  - Development CEASED: lack of differentiation for payers
- **PF-734**: diabetes
Pharmaceutical Research and Development is Evolving

**PAST**

- Regulatory Need

**PRESENT**

- Regulatory Need
- Payer Need
Regulatory Review & Approval
Phase III
1,000–5,000 patient volunteers used to monitor adverse reactions to long-term use

Phase I
20–80 healthy volunteers used to determine safety and dosage

Preclinical Testing
Laboratory and Animal Testing

Phase II
100–300 patient volunteers used to look for efficacy and side effects

Phase III
1,000–5,000 patient volunteers used to monitor adverse reactions to long-term use

Public Reimbursement

Generic Entry

Length of time in years

Discovery

Aligned with the needs of the healthcare system. Horizon scanning of what society needs. Validate disease and pathways

Early Engagement with Payers

• “Ways need to be found to develop partnerships that link researchers, industry, governments, policy makers, and health system managers so that the fruits of innovation are quickly and appropriately taken into health systems and reach those that need them”.

Organisation for Economic Co-operation and Development
Translating Discoveries into New and Better Therapies

Better understanding of disease/drug mechanisms

More efficient drug discovery and development

Better medicines, faster

Health benefits for patients

Understanding human physiology

Pre-competitive collaborative research

Public investment

Private investment

‘-omics’

ICT

Image

Imaging

Pfizer
Early Discovery

MaRS EXCITE

SGC
A public-private partnership that supports the discovery of new medicines through open access research.

238 Int. J. Technology Transfer and Commercialisation, Vol. 9, No. 3, 2010

Commercialisation of innovations from the UK National Health Service

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Sheffield S1 1WB, UK
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*Corresponding author
- Feedback prior to phase 3 lock
- Study design; comparator, endpoints, follow-up period, other data gaps

http://www.nice.org.uk/aboutnice/scientificadvice/AboutScientificAdvice.jsp
Ways that HTA Can Shape the R&D Process

Not always in the toolkit yet important

Currently in the HTA toolkit:

- Certainty of evidence and design of pivotal studies
  - Endpoint
  - Comparator
  - Follow-up
  - Generic QoL measures
- Economic evaluation and budget impact

- Patient/caregiver relevant outcomes and preferences
- Feasibility and health technology management plans (how to introduce and adopt the technology optimally)
- Further evidence gathering plans (?phase 4)
- Burden of Disease
- Areas of unmet need
- Ethical considerations
- Labour workforce impact and productivity
In Conclusion…

• The R&D process is becoming more complex and risky.
• The few medicines coming out R&D need to meet society and payers needs.
• New models of collaboration between all stakeholders are being put in place to address the innovation gap.
• Such models are urgently required between the Biopharma sector and payers/HTA bodies.
• HTA has matured into a pivotal component of the R&D continuum.
• HTA has the potential to become ‘dynamic’, it can guide R&D, manage optimal adoption of health technologies, contribute to the knowledge base and act as a conduit for future innovations.